Application No.: 10/721,253

IN THE CLAIMS:

This following listing of claims will replace all prior versions, and listings of claims in the application.

1. (Currently Amended) A method of monitoring calibration of a spectrophotometric apparatus comprising one or more <u>than one calibration algorithm</u> <u>calibration algorithms</u> for one or more than one analyte analytes comprising:

i) measuring absorbance of a quality control material with said apparatus to obtain a measurement, said quality control material exhibiting an absorbance spectra characterized as having a negative slope for a continuous spectral segment from about 5 nm to about 200 nm in length said spectral segment including a principal calibration wavelength for said one or more than one analyte analytes;

- ii) calculating one or more <u>than one value values</u> from said measurement using said one or more <u>than one calibration algorithm calibration algorithms</u>; and
- iii) comparing said one or more than one value values with an assigned value given to said quality control material for each of said one or more than one analyte analytes, thereby monitoring said one or more than one calibration algorithms of said apparatus.
- 2. (Currently Amended) The method of claim 1, wherein said one or more than one analyte analytes is one or more than one analyte analytes in a biological fluid selected from the group consisting of serum, plasma, urine, synovial fluid and cerebrospinal fluid.

Application No.: 10/721,253

nm to about 600 nm.

3. (Currently Amended) The method of claim 2, wherein said one or more than one analyte analytes is bilirubin, and in said step of measuring (step i)) said spectral segment is selected from wavelengths of said absorbance spectra of from about 450

- 4. (Currently Amended) The method of claim 2, wherein said one or more <u>one analyte</u> analytes is an indicator of hemolysis, and in said step of measuring (step i)) said spectral segment is selected from wavelengths of said absorbance spectra of from about 550 nm to about 650 nm, said indicator of hemolysis selected from the group consisting of <u>total hemoglobin</u> (total Hb) total Hb, <u>oxy-hemoglobin</u> (Oxy-Hb) Oxy-Hb, and "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb".
- 5. (Currently Amended) The method of claim 2, wherein said one or more than one analyte analytes is a hemoglobin-based blood substitute, and in said step of measuring (step i)) said spectral segment is selected from wavelengths of said absorbance spectra of from about 550 nm to about 700 nm.
- 6. (Currently Amended) The method of claim 2, wherein said one or more than one analyte analytes is met-hemoglobin, and in said step of measuring (step i)) said spectral segment is selected from wavelengths of said absorbance spectra of from about 610 nm to about 690 nm.

Application No.: 10/721,253

7. (Currently Amended) The method of claim 2, wherein said one or more than one analyte analytes is methylene blue, and in said step of measuring (step i)) said spectral segment is selected from wavelengths of said absorbance spectra of from about 650 nm to about 750 nm.

- 8. (Currently Amended) The method of claim 2, wherein said one or more than one analyte analytes is biliverdin, and in said step of measuring (step i)) said spectral segment is selected from wavelengths of said absorbance spectra of from about 650 nm to about 800 nm.
- 9. (Currently Amended) A method of monitoring calibration of a spectrophotometric apparatus comprising one or more <u>than one calibration algorithm</u> <u>calibration algorithms</u> for a <u>perflurocarbon</u> <u>perfluorocarbon</u>-like blood substitute, turbidity, or a combination thereof, wherein said turbidity is measured in concentration units of a lipid emulsion, comprising:
- i) measuring absorbance of a quality control material with said apparatus to obtain a measurement, said quality control material exhibiting an absorbance spectra within the range from about 700 nm to about 1100 nm;
- ii) calculating one or more <u>than one value values</u> from said measurement using said one or more than one calibration algorithm calibration algorithms; and
- iii) comparing said one or more than one value values with an assigned value given to said quality control material for each of said perflurocarbon perfluorocarbon-like blood substitute, said turbidity, or a combination thereof; thereby monitoring said one or

Application No.: 10/721,253

more than one calibration algorithm calibration algorithms of said apparatus.

10. (Currently Amended) A method of monitoring calibration of a spectrophotometric apparatus comprising one or more <u>than one calibration algorithm calibration algorithms</u> for a <u>perflurocarbon perfluorocarbon</u>-like blood substitute, turbidity, or a combination thereof wherein said turbidity is measured in concentration units of a lipid emulsion,

comprising:

i) measuring absorbance of a quality control material with said apparatus to obtain a measurement, said quality control material exhibiting an absorbance spectra characterized as having a negative slope for a continuous spectral segment from about 5 nm to about 400 nm within the range of the absorbance spectra from about 700 nm to about 1100 nm:

ii) calculating one or more than one value values from said measurement using said one or more than one calibration algorithm calibration algorithms; and

iii) comparing said one or more <u>than one value values</u> with an assigned value given to said quality control material for said one or more <u>than one</u> of a <u>perflurocarbon</u> <u>perfluorocarbon</u>-like blood substitute, turbidity, or a combination thereof, wherein said turbidity is measured in units of a lipid emulsion; thereby monitoring said one or more than one calibration algorithm <u>calibration algorithms</u> of said apparatus.

11. (Currently Amended) The method of claim 1, wherein said quality control material comprises one or more than one susbstance substances, said one or more than one substance substance substance substances selected from the group consisting of a dye, copper sulfate, total

Application No.: 10/721,253

hemoglobin (total-Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb, carboxy-hemoglobin (carboxy-Hb) earboxy-Hb, "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb", cyanmet-hemoglobin (cyanmet-Hb) cyanmet-Hb, a Hb hemoglobin-based blood substitute, a lipid emulsion, and a perflurocarbon perfluorocarbon-like blood substitute.

- 12. (Currently Amended) The method of claim 9, wherein said quality control material further comprises one or more than one substance substances, said one or more than one substance substances selected from the group consisting of a dye, copper sulfate, total hemoglobin (total-Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb, carboxy-hemoglobin (carboxy-Hb) carboxy-Hb, "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb", cyanmet-hemoglobin (cyanmet-Hb) cyanmet-Hb, a Hb hemoglobin-based blood substitute, a lipid emulsion, and a perflurocarbon perfluorocarbon-like blood substitute.
- 13. (Currently Amended) The method of claim 10, wherein said quality control material further comprises one or more than one substance substances, said one or more than one substance substances selected from the group consisting of a dye, copper sulfate, total hemoglobin (total-Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb, carboxy-hemoglobin (carboxy-Hb) earboxy-Hb, "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb", cyanmet-hemoglobin (cyanmet-Hb) eyanmet-Hb, a Hb hemoglobin-based blood substitute, a lipid emulsion, and a perfluerocarbon perfluorocarbon-like blood substitute.

Application No.: 10/721,253

14. (Currently Amended) The method of claim 11, wherein said absorbance spectra of

said one or more than one substance substances is altered by adding a spectral

modifier.

15. (Original) The method or claim 14, wherein said modifier causes a non-additive

spectral shift in said absorbance spectra.

16. (Original) The method of claim 15, wherein said modifier is selected from the group

consisting of a polymer, a protein, amaranth, and a combination thereof.

17. (Currently Amended) The method of claim 16, wherein said polymer is selected from

the group consisting of polyvinylpyrrolidone (PVP) PVP and polyethylene glycol (PEG)

PEG.

18. (Currently Amended) A reagentless method for determining the concentration of one

or more than one analyte analytes in a sample in a spectrophotometric apparatus

comprising at least one primary calibration algorithm comprising:

i) monitoring calibration of said apparatus as defined in claim 1;

ii) measuring absorbance values of said sample;

iii) calculating an order derivative of absorbance of said sample; and

iv) calculating a concentration of said one or more than one analyte analytes in

said sample, by applying said at least one primary calibration algorithm to said order

Application No.: 10/721,253

derivative of absorbance value.

19. (Currently Amended) A reagentless method for determining the concentration of one

or more than one analyte analytes in a sample in a spectrophotometric apparatus

comprising at least one primary calibration algorithm comprising:

i) monitoring calibration of said apparatus as defined in claim 9;

ii) measuring absorbance values of said sample;

iii) calculating an order derivative of absorbance of said sample; and

iv) calculating a concentration of one or more than one of said perflurocarbon

perfluorocarbon-like blood substitute, said turbidity, or a combination thereof, in terms of

concentration of a lipid emulsion in said sample, by applying said primary calibration

algorithm to said order derivative of absorbance value.

20. (Currently Amended) A reagentless method for determining the concentration of one

or more than one analyte analytes in a sample in a spectrophotometric apparatus

comprising at least one primary calibration algorithm comprising:

i) monitoring calibration of said apparatus as defined in claim 10;

ii) measuring absorbance values of said sample;

iii) calculating an order derivative of absorbance of said sample; and

iv) calculating a concentration of one or more than one of said perflurocarbon

perfluorocarbon-like blood substitute, said turbidity, or a combination thereof, in terms of

concentration of a lipid emulsion in said sample, by applying said primary calibration

algorithm to said order derivative of absorbance value.

-11-

Application No.: 10/721,253

21. (Currently Amended) The method of claim 18, wherein said one or more than one

analyte analytes is one or more than one analyte analytes in a biological fluid selected

from the group consisting of whole blood, serum, plasma, urine, synovial fluid and

cerebrospinal fluid.

22. (Currently Amended) The method of claim 21, wherein said one or more than one

analyte analytes is bilirubin, and said spectral segment is selected from wavelengths of

said absorbance spectra of from about 450 nm to about 600 nm.

23. (Currently Amended) The method of claim 21, wherein said one or more than one

analyte analytes is an indicator of hemolysis, and said spectral segment is selected

from wavelengths of said absorbance spectra of from about 550 nm to about 650 nm,

said indicator of hemolysis selected from the group consisting of total hemoglobin (total-

Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb, and "total hemoglobin minus met-

hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb".

24. (Currently Amended) The method of claim 21, wherein said one or more than one

analyte analytes is a hemoglobin-based blood substitute, and said spectral segment is

selected from wavelengths of said absorbance spectra of from about 550 nm to about

700 nm.

Application No.: 10/721,253

25. (Currently Amended) The method of claim 21, wherein said one or more than one analyte analytes is met-hemoglobin, and said spectral segment is selected from wavelengths of said absorbance spectra of from about 610 nm to about 690 nm.

- 26. (Currently Amended) The method of claim 21, wherein said one or more <u>than one</u> analyte analytes is methylene blue, and said spectral segment is selected from wavelengths of said absorbance spectra of from about 650 nm to about 750 nm.
- 27. (Currently Amended) The method claim 21, wherein said one or more than one analyte analytes is biliverdin, and said spectral segment is selected from wavelengths of said absorbance spectra of from about 650 nm to about 800 nm.
- 28. (Currently Amended) The method of claim 18, wherein said quality control material comprises one or more than one substance substances selected from the group consisting of a dye, copper sulfate, total hemoglobin (total-Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb, carboxy-hemoglobin (carboxy-Hb) earboxy-Hb, "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb", cyanmet-hemoglobin (cyanmet-Hb) eyanmet-Hb, a Hb hemoglobin-based blood substitute, a lipid emulsion, and a perflurocarbon perfluorocarbon-like blood substitute.
- 29. (Currently Amended) The method of claim 28, wherein said absorbance spectra of said one or more than one substance substances is altered by adding a spectral modifier.

Attorney Docket No.: 026806.00011

Amendment Under C.F.R. § 1.111 Application No.: 10/721,253

30. (Original) The method of claim 29, wherein said modifier causes a non-additive spectral shift in said absorbance spectra.

- 31. (Original) The method of claim 30, wherein said modifier is selected from the group consisting of a polymer, a protein, and amaranth.
- 32. (Currently Amended) The method of claim 31, wherein said polymer is selected from the group consisting of polyvinylpyrrolidone (PVP) PVP and polyethylene glycol (PEG)

 PEG.
- 33. (Currently Amended) A method for selecting one or more than one substance substances as a quality control material for monitoring at least one primary calibration algorithm on a spectrophotometric apparatus comprising:
- i) identifying a principal calibration wavelength for each of one or more than one analyte analytes;
- ii) screening absorption spectra of said one or more <u>than one substance</u> substances; and
- iii) selecting one or more than one of said substances exhibiting a negative slope of said absorbance spectra, for a continuous spectral segment from about 5 nm to about 200 nm in length, said spectral segment including said principal calibration wavelength.

Application No.: 10/721,253

34. (Currently Amended) The method of claim 33, wherein said one or more than one analyte analytes is one or more than one analyte analytes in a biological fluid selected from the group consisting of serum, plasma, urine, synovial fluid and cerebrospinal fluid.

- 35. (Currently Amended) The method of claim 34, wherein said one or more than one analyte analytes is bilirubin, and in said step of selecting (step iii)), said spectral segment is selected from wavelengths of said absorbance spectra of from about 450 nm to about 600 nm.
- 36. (Currently Amended) The method of claim 34, wherein said one or more <u>than one</u> <u>analyte analytes</u> is an indicator of hemolysis, and in said step of selecting (step iii), said spectral segment is selected from wavelengths of said absorbance spectra of from about 550 nm to about 650 nm, said indicator of hemolysis selected from the group consisting of <u>total hemoglobin</u> (total-Hb) total Hb, <u>oxy-hemoglobin</u> (Oxy-Hb) Oxy-Hb, and "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb").
- 37. (Currently Amended) The method of claim 34, wherein said one or more <u>than one</u> <u>analyte analytes</u> is a hemoglobin-based blood substitute, and in said step of selecting (step iii)), said spectral segment is selected from wavelengths of said absorbance spectra of from about 550 nm to about 700 nm.
- 38. (Currently Amended) The method of claim 34, wherein said one or more than one analyte analytes is met-hemoglobin, and in said step of selecting (step iii)), said spectral

-15-

TECH/405903.1

Application No.: 10/721,253

segment is selected from wavelengths of said absorbance spectra of from about 610 nm to about 690 nm.

39. (Currently Amended) The method of claim 34, wherein said one or more than one analyte analytes is methylene blue, and in said step of selecting (step iii)), said spectral segment is selected from wavelengths of said absorbance spectra of from about 650 nm to about 750 nm.

40. (Currently Amended) The method of claim 34, wherein said one or more than one analyte analytes is biliverdin, and in said step of selecting (step iii)), said spectral segment is selected from wavelengths of said absorbance spectra of from about 650 nm to about 800 nm.

- 41. (Currently Amended) The method of claim 33, wherein said quality control material comprises one or more than one substance substances, said one or more than one substance substance substances selected from the group consisting of a dye, copper sulfate, total hemoglobin (total-Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb, carboxy-hemoglobin (carboxy-Hb) earboxy-Hb, "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb", cyanmet-hemoglobin (cyanmet-Hb) eyanmet-Hb, a Hb hemoglobin-based blood substitute, a lipid emulsion, and a perflurocarbon perfluorocarbon-like blood substitute.
- 42. (Currently Amended) The method of claim 33 wherein in said step of identifying

Application No.: 10/721,253

(step i)), said principal calibration wavelength of said analyte, and in said step of screening (step ii)) said absorption spectra of said one or more than one substance substances, are obtained on said spectrophotometric apparatus having one or more than one primary calibration algorithm algorithms.

- 43. (Currently Amended) A method for selecting one or more than one substance substances as a quality control material for monitoring at least one primary calibration algorithm on a spectrophotometric apparatus for one or more than one of a perflurocarbon perfluorocarbon-like blood substitute and turbidity, wherein turbidity is measured in terms of concentration units of a lipid emulsion, comprising:
- i) identifying a principal calibration wavelength for each of one or more <u>than one</u> of said <u>perflurocarbon</u> perfluorocarbon-like blood substitute and said turbidity;
- ii) screening absorption spectra of said one or more <u>than one substance</u> substances; and
- iii) selecting one or more <u>than one</u> of said substances exhibiting absorbance within the range from about 700 nm to about 1100 nm.
- 44. (Currently Amended) A method for selecting one or more than one substance substances as a quality control material for monitoring at least one primary calibration algorithm on a spectrophotometric apparatus for one or more than one of a perflurocarbon perfluorocarbon-like blood substitute and turbidity wherein turbidity is measured in terms of concentration units of a lipid emulsion, comprising:

Application No.: 10/721,253

i) identifying a principal calibration wavelength for each of one or more <u>than one</u> of said <u>perflurocarbon</u> <u>perfluorocarbon</u>-like blood substitute and said turbidity;

- ii) screening absorption spectra of said one or more <u>than one substance</u> substances; and
- iii) selecting one or more <u>than one</u> of said substances exhibiting absorbance spectra as having a negative slope for a continuous spectral segment from about 5 nm to about 400 nm within the range of wavelengths from about 700 nm to about 1100 nm.

45.-51. (Cancelled)

- 52. (Currently Amended) A quality control material for monitoring the calibration algorithms for two or more <u>than two</u> analytes comprising, one or more <u>than one</u> <u>substance substances</u> having a combined absorption spectrum exhibiting a negative slope for one or more <u>than one</u> continuous spectral segment, wherein each of said one or more <u>than one</u> continuous spectral segment is from about 5 nm to 200 nm in length, and wherein said one or more <u>than one</u> continuous spectral segment includes one or more than <u>one</u> principal calibration wavelengths, for said two or more <u>than two</u> analytes.
- 53. (Currently Amended) The quality control material of claim 52, wherein one of said two or more <u>than two</u> analytes is bilirubin, and said spectral segment is selected from wavelengths of said absorbance spectra of from about 450 nm to about 600 nm.
- 54. (Currently Amended) The quality control material of claim 52, wherein one of said -18-

TECH/405903.1

Attorney Docket No.: 026806.00011

Amendment Under C.F.R. § 1.111 Application No.: 10/721,253

two or more than two analytes is an indicator of hemolysis, and said spectral segment is selected from wavelengths of said absorbance spectra of from about 550 nm to about 650 nm, said indicator of hemolysis selected from the group consisting of total hemoglobin (total-Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb, and "total hemoglobin minus met-hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb".

55. (Currently Amended) The quality control material of claim 52, wherein said two or more than two analytes are two or more than two analytes in a biological fluid selected from the group consisting of whole blood, serum, plasma, synovial fluid, cerebrospinal fluid, urine, mucus, lymphatic fluid, semen and feces.

56. (Currently Amended) The quality control material of claim 52, wherein one of said two or more than two analytes is a hemoglobin-based blood substitute, and said spectral segment is selected from wavelengths of said absorbance spectra of from about 550 nm to about 700 nm.

57. (Currently Amended) The quality control material claim 52, wherein one of said two or more than two analytes is met-hemoglobin, and said spectral segment is selected from wavelengths of said absorbance spectra of from about 610 nm to about 690 nm.

58. (Currently Amended) The quality control material claim 52, wherein one of said two or more than two analytes is methylene blue, and said spectral segment is selected

Application No.: 10/721,253

from wavelengths of said absorbance spectra of from about 650 nm to about 750 nm.

59. (Currently Amended) The quality control material claim 52, wherein one of said two

or more than two analytes is biliverdin, and said spectral segment is selected from

wavelengths of said absorbance spectra of from about 650 nm to about 800 nm.

60. (Currently Amended) The quality control material claim 52, wherein one of said two

or more than two analytes is either a simulator of turbidity or a perflurocarbon

perfluorocarbon-like blood substitute, said quality control material further characterized

as having an absorbance spectrum within the range of from about 700 nm to about

1100 nm.

61. (Currently Amended) The quality control material claim 52, wherein one of said two

or more than two analytes is either a simulator of turbidity or a perflurocarbon

perfluorocarbon-like blood substitute, said absorption spectrum of said quality control

material further characterized as having a negative slope for a continuous spectral

segment from about 5 nm to about 400 nm within the range of from about 700 nm to

about 1100 nm.

62. (Currently Amended) The quality control material of claim 52, further comprising one

or more than one substance substances selected from the group consisting of a dye

copper sulfate, total hemoglobin (total-Hb) total Hb, oxy-hemoglobin (Oxy-Hb) Oxy-Hb,

carboxy-hemoglobin (carboxy-Hb) carboxy-Hb, "total hemoglobin minus met-

-20-

Application No.: 10/721,253

hemoglobin" ("total Hb minus met-Hb") "total Hb minus met-Hb", cyanmet-hemoglobin

(cyanmet-Hb) eyanmet-Hb, a Hb hemoglobin-based blood substitute, a lipid emulsion, a

perflurocarbon perfluorocarbon-like blood substitute, and a combination thereof.

63. (Currently Amended) The quality control material of claim 60, wherein an absorbance spectrum of said one or more than one substance substances is altered by adding a spectral modifier.

64. (Original) The quality control material of claim 63, wherein said modifier causes a non-additive spectral shift in said absorbance spectra.

65. (Original) The quality control material of claim 64, wherein said modifier is selected from the group consisting of a polymer, a protein, and amaranth.

66. (Currently Amended) The quality control material of claim 65, wherein said polymer is selected from the group consisting of polyvinylpyrrolidone (PVP) PVP and polyethylene glycol (PEG) PEG.

67.-96. (Cancelled)

97. (Currently Amended) The quality control material of claim 62, wherein said one or more than one substance substances is not supplemented with bilirubin.